REMARKS

A. Regarding the Amendments

Claims 67 and 91 have been amended to claim the subject matter of the present invention with greater specificity and particularity. More specifically, claims 67 and 91 have been amended to recite additional tautomers and isomers. The matter added to claims 67 and 91 was disclosed in the originally filed application (see, page 6, lines 10-14). No new matter has been added.

The Applicant acknowledges the withdrawal of the previous rejections under 35 U.S.C. § 103(a) over Naviaux et al. and over Page et al. Upon entry of this amendment, claims 67, 70, 73-81, 84-91, and 95-110 will be under consideration.

B. Rejections Under 35 U.S.C. § 103 (a)

Claims 67, 70, 73-81, 84-91, and 95-110 stand rejected under 35 U.S.C. § 103(a) as allegedly being obvious over Page et al., "Developmental Disorder Associated with Increased Cellular Nucleotidase Activity," *Proc. Natl. Acad. Sci. USA*, vol. 94, pp. 11601-11606 (1997) in view of Elverland et al., "Audiological Findings in a Family with Mitochondrial Disorder," *American Journal of Otology*, vol. 12, No. 6, pp. 459-465 (November 1991), abstract only is cited (page 3, third paragraph of the Office Action). The rejection is respectfully traverse on the following grounds.

The standard that has to be satisfied for making a *prima facie* case of obviousness was provided previously (see the Response to the Office Action, filed December 12, 2005). The Applicant submits that the criteria of this standard have not been met, either in view of Page et al. or Elverland et al. or a combination of the teachings thereof.

Page et al. disclose treatment of various developmental disorders, but fails to disclose or suggest treatment of specific disorders, diseases, or pathologies recited in

claims 67 and 91. To cure this deficiency of Page et al., the Examiner has proposed to combine Page et al. and Elverland et al.

The Examiner has reasoned that Page et al. teach the treatment of various syndromes characterized by abnormal purine and pyrimidine metabolism using uridine, but fail to disclose that what is treated are various mitochondrial disorders. The Examiner further states that what is claimed in claim 67 and 91 is directed not to "actual mitochondrial diseases" but to "clinical features" such as renal tubular acidosis, lactic acidemia, encephalomyopathy, aminoaciduria, etc. (see page 4, lines 1-6 of the Office Action). Therefore, according to the Examiner, what is taught by Page et al. makes the subject matter of claim 67 and 91 obvious in view of Elverland et al., because Elverland et al. teaches that a mitochondrial disorder is an "inborn error of metabolism" affecting the cellular respiratory chain. While the Examiner may be correct in her analysis of the teachings of Elverland et al., it is respectfully submitted that these teachings are insufficient to make a *prima facie* case of obviousness.

As discussed previously, each of claims 67 and 91 recites the treatment of

> "mitochondrial renal tubular acidosis,
> multiple mitochondrial deletion syndrome,
> Leigh syndrome, lactic acidemia,
> 3-hydroxybutyric acidemia, encephalomyopathy,
> 1+proteinuria, pyruvate dehydrogenase deficiency,
> complex I deficiency, complex IV deficiency,
> aminoaciduria, hydroxyprolinuria, and
> MARIAHS syndrome."

Contrary to the Examiner's belief, as mentioned above, those skilled in the art would clearly understand that each of conditions recited in claims 67 and 91 is a genuine disease, not just a "clinical feature." For example, referring to some disorders specifically mentioned by the Examiner, renal tubular acidosis is a disease that occurs when the kidneys fail to excrete acids into the urine, which causes a person's blood to remain too acidic. Without proper treatment, chronic acidity of the blood leads to growth

retardation, kidney stones, bone disease, and progressive renal failure. Lactic acidemia is a blood disorder characterized by an increased acidity of blood, the pH of which falls below 7, caused by accumulation of lactic acid more rapidly than it can be metabolized. Encephalomyopathy is any of a group of diseases characterized by abnormal mitochondrial function with involvement of the central nervous system and skeletal muscle and, in most cases, lactic acidosis. Aminoaciduria is a metabolic defect or disorder that is characterized by abnormal presence of amino acids in the urine. 1+proteinuria is a kidney disease characterized by excessive excretion of protein in urine.

The Applicant respectfully represents that neither the definitions of the above diseases nor the fact that they are real diseases can be reasonably disputed. The Applicant also respectfully submits that Page et al. neither disclose nor suggest the treatment of any of these disorders or diseases. What Page et al. do disclose is the treatment of four patients having various developmental disorders. There is no detailed description of the disorders except for their manifestations. These manifestations are discussed in terms of very broad clinical categories such as behavioral, speech, neurological, immunological, etc. For example, page et al. describe such manifestations as seizures, ataxia, an awkward gait, mildly impaired motor control, hyperactivity, distractability, deliriousness, an abnormal social interaction, etc.

Page et al. fail to provide any disclosure or any suggestion linking any of these manifestations to any specific disease or disorder recited in claims 67 and 91. One skilled in the art would know that the same or similar outward manifestations may characterize various diseases, not just one disease. For instance, URNS is a specific disorder but not one of the specific disorders that is recited in the claims, and there is no evidence that the treatment of URNS described by Page et al. would t have motivated one skilled in the art to treat any of the different claimed disorders.

As a further illustration, just because Page et al. provide some guidance with respect to the treatment of some conditions clinically presented as hyperactivity, does not

mean that such guidance can be applied to the treatment of a person suffering from a disease recited in claims 67 and 91. Therefore, it is respectfully submitted that one having ordinary skill in the art will not be motivated to use the methods discussed in page et al. and to modify then so as to make them applicable to the treatments recited in claims 67 and 91.

For example, some diseases listed in claims 67 and 91 are kidney disorders or are related to diabetes, as can be easily understood by those skilled in the art. In other words, just because Page et al. described using uridine for treating various developmental disorders, this does not make it obvious to one skilled in the art to use uridine for treating kidney disease, 1+proteinuria, or diabetes, for example.

Elverland et al. fail to cure these deficiencies of Page et al. and to link the disclosure of Page et al. to general mitochondrial disorders, beyond the developmental problems addressed by Page e t al. More specifically, all that is disclosed in Elverland et al. is that many mitochondrial disorders are inborn and that the defects in energy production can lead to a variety of clinical manifestations. Specific kinds of the disorders on which Elverland et al. concentrate are hearing loss and similar audiological problems. There is no suggestion or indeed any mentioning in Elverland et al. that might motivate one skilled in the art to apply the therapy proposed in Page et al. (i.e., uridine treatments) to treating any disorders and diseases listed in claims 67 and 91.

In view of the foregoing, it is respectfully submitted that each of claims 67 and 91 is patentably distinguishable over Page et al. in view of Elverland et al. Each of claims 70, 73, 73-81, 84-90, and 95-110 depends, directly or indirectly, either on claim 67 or on claim 91, and is allowable for at least the same reason. Reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, reconsideration and favorable action on all claims are respectfully requested. In the event any matters remain to be resolved, the Examiner is requested to contact the undersigned at the telephone number given below so that a prompt disposition of this application can be achieved.

Check number 584584 in the amount of $60.00 is enclosed as payment for the Petition for a One-Month Extension of Time fee. No other fee is deemed necessary with the filing of this response. However if any fees are due, the Commissioner is hereby authorized to charge any fees, or make any credits, to Deposit Account No. 07-1896 referencing the above-identified attorney docket number. A copy of the Transmittal Sheet is enclosed.

Respectfully submitted,

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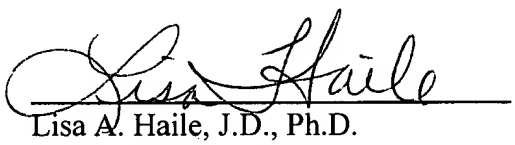

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